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Cutaneous Leishmania aethiopica diagnosed in the United States

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Abstract

Cutaneous leishmaniasis is a parasitic infection caused by certain *Leishmania* spp and is endemic in the New world (Central and South America) and Old World (Africa and the Middle East) where it is transmitted via sandflies of the *Phlebotomus* and *Lutzomyia* species. We describe a case of a 61-year-old woman who presented with an asymptomatic red-brown papule on her lower back approximately one year after returning to the United States from a trip to Ethiopia and Cameroon. Polymerase chain reaction was performed on the biopsy material and identified *Leishmania aethiopica*. This case highlights an atypical location and demonstrates how to accurately diagnose and treat this parasitic infection.

Keywords: amastigotes, Cameroon, cutaneous leishmaniasis, Ethiopia, Leishmania aethiopica, sandfly

Introduction

Cutaneous leishmaniasis (CL) is the result of a parasitic infection caused by trypanosomes in the genus *Leishmania*. Mammals are the main reservoir hosts for *Leishmania* spp, and the trypanosomes are transmitted between hosts via the feeding of female sandflies of the *Phlebotomus* and *Lutzomyia* species. *Leishmania* spp are endemic to the tropical and subtropical regions of Central and South America, Africa, the Middle East, and Asia [1,2]. Of note, there have also been reports of minor endemic spread in isolated communities in the United States (Texas and Oklahoma) beginning in the 1990s [3]. It is estimated that there are 700,000-1.2 million new cases per year worldwide of all *Leishmania* species [1].

Case Synopsis

A 61-year-old woman was evaluated 6 months after developing a slightly raised, non-painful, non-pruritic red-brown lesion on her left lower back (**Figure 1**). The patient reported travel to Cameroon and Ethiopia approximately 8 months prior to noticing the lesion, during which time she denied any insect exposures. The patient was otherwise healthy with a past medical history of osteoarthritis and high blood pressure. The patient's medications

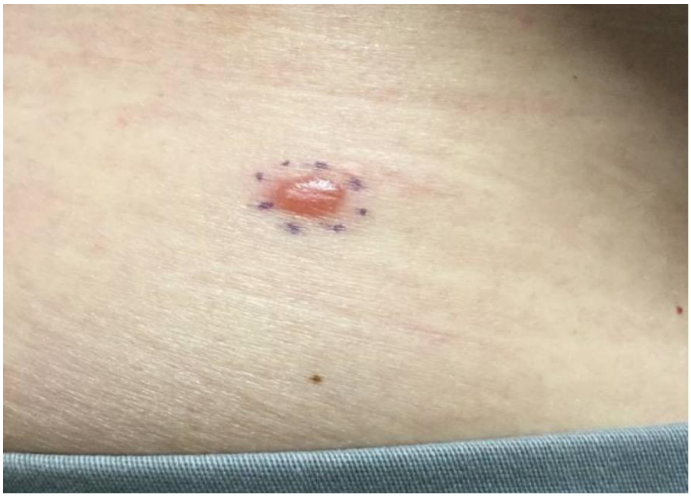

Figure 1. *Red-brown well circumscribed nodule on patient's lower left back at time of diagnosis (demarcated with purple ink).*

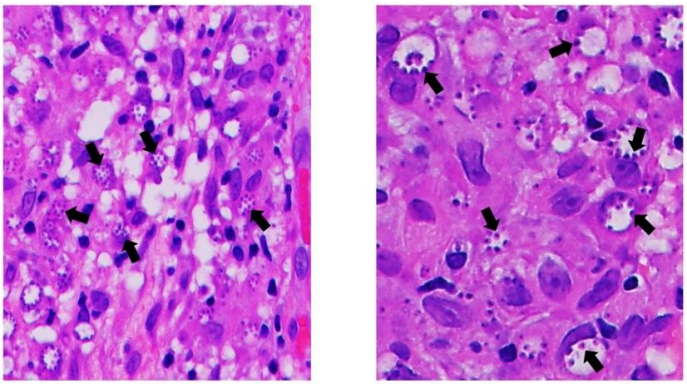

Figure 2. *Punch biopsy obtained from active border of lower back lesion demonstrating innumerous intracellular amastigotes. Arrows denote clusters of amastigotes inside histiocytes. H&E, 20× and 40×.*

included hydrochlorothiazide, losartan, and meloxicam. Her review of systems was negative and cutaneous examination revealed a single 9×5mm red brown smooth papule on the patient's left lower back. No scabbing or ulceration was noted. No other skin lesions were noted. A shave biopsy of the papule was obtained and histologic sections revealed a dense dermal histiocytic infiltrate containing numerous amastigotes (**Figure 2**), which was consistent with cutaneous leishmaniasis of unknown species. One week later, a punch biopsy was performed and was sent to the Center for Disease Control (CDC) for culture in Novy-McNeal-Nicolle (NNN) medium that yielded promastigotes after several weeks (Process outlined in **Figure 3**). Species-specific polymerase chain reaction was positive for these identified *Leishmania aethiopica*, which is endemic to Ethiopia. The patient was referred to an infectious disease consultant who recommended clinical monitoring since the patient only had one localized cutaneous lesion. Follow up four months later revealed that the papule remained red-brown in coloration, but had diminished slightly in size. The patient reported some mild pruritus (**Figure 4**).

Case Discussion

Leishmania aethiopica is endemic to Ethiopia and Mount Elgon in Kenya, with some studies finding up to 65.4% of the population in these areas as having an active or past leishmaniasis infection [4]. When humans are bitten by infected sandflies, flagellated promastigotes are delivered into the tissues and phagocytosed by macrophages or dendritic cells, wherein they transform into the replicative amastigotes. These eventually overburden host macrophages, escaping into surrounding tissue and induce a localized host immune response [2,5]. In CL the initial bite presents first as a small erythematous macule which progresses to become a papule that in

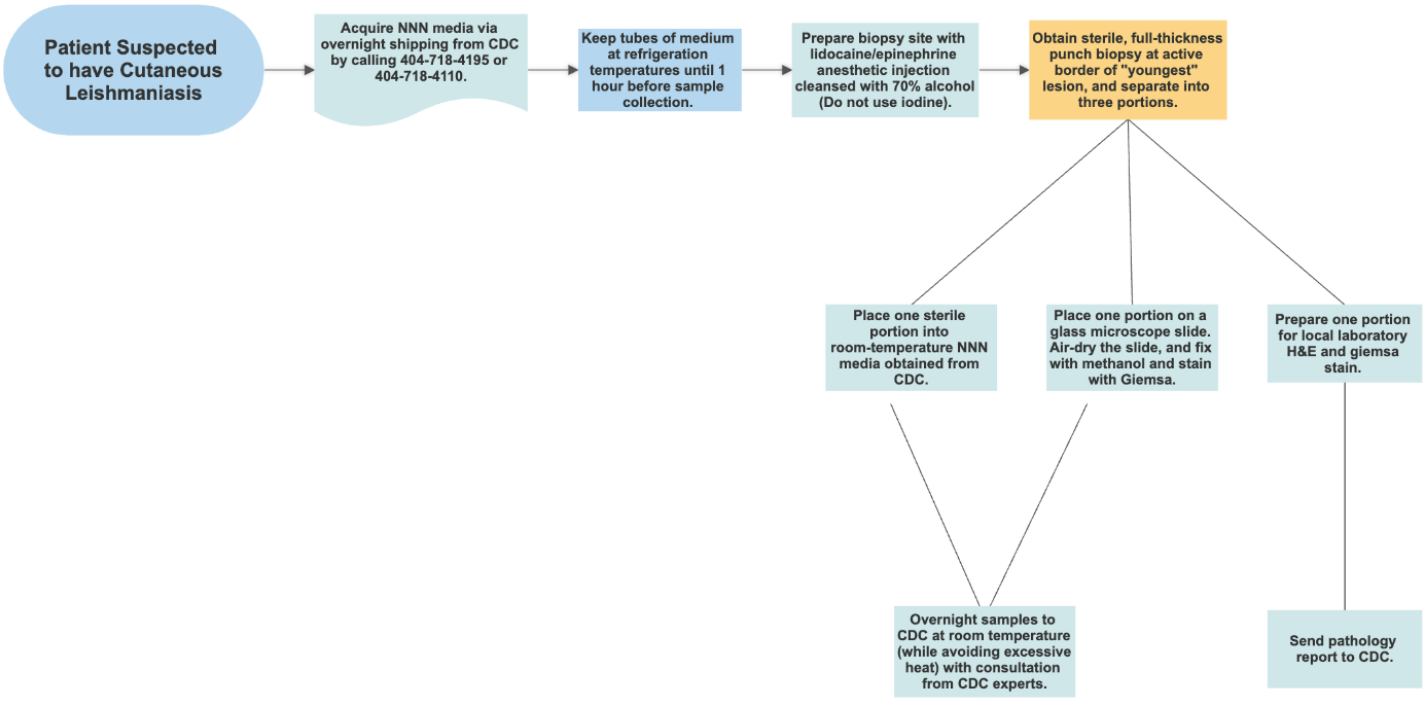

Figure 3. *Process overview for sending a suspected cutaneous leishmaniasis sample to Center for Disease Control (CDC).*

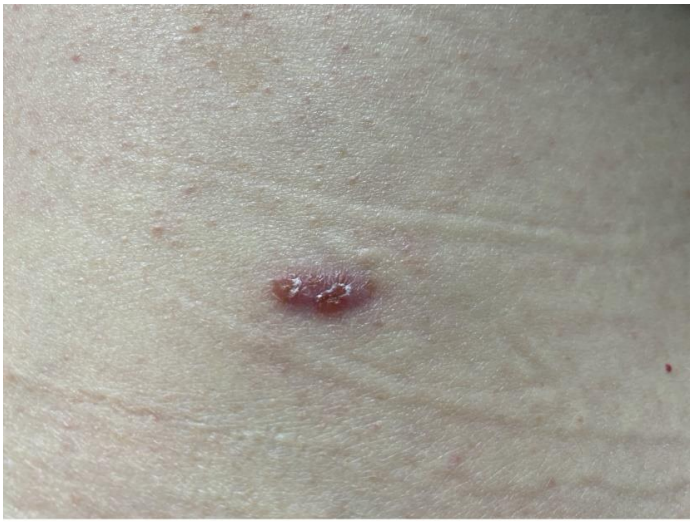

Figure 4. *Cutaneous leishmaniasis on patient's lower left back, four months after diagnosis.*

most cases progressively ulcerates over the next two weeks to six months as the host produces a Th1/Th2-mediated immune response [6]. Lesions will usually spontaneously heal over many months, leaving a permanent atrophic scar [5]. Although it is suggested that resolution of primary infection provides immunity to future leishmaniasis infections [9], one study found that 2.5% of children in an Ethiopian village with a healed CL lesion also had an active CL lesion, indicating that the immunologic response does not provide full protection against future infections. However, it is unclear if the children were infected with the same species as the initial infection [4].

The presentation in our patient was atypical for *Leishmania aethiopica* owing to the fact that this patient's lesion appeared on the trunk. It has been reported that 45-97% of CL lesions appear on the head and neck, with nearly all other lesions being found on the arms and legs because of the typical sandfly exposure of these areas [10]. Although the patient does not recall being bitten or having this area exposed, we postulate that the patient was bitten while bathing or sleeping. Therefore, it is essential that clinicians perform full-body skin examinations when evaluating patients for CL. In most immunocompetent patients, lesions will resolve leaving behind only a scar in the months following ulceration. However, *Leishmania aethiopica* has a slower healing time than most other *Leishmania* spp [10]. A major concern of infection with *Leishmania aethiopica* is the possibility of developing diffuse cutaneous leishmaniasis, which presents as a single or multiple lesions that can grow for years or even decades [11]. Therefore, it is essential to monitor patients for continued lesion growth beyond 6 months [11].

A common parenteral treatment—used for decades in Ethiopian villages—is intravenous (IV) sodium stibogluconate, an antimony derivative. Sodium stibogluconate was shown in a small study to lead to disappearance of inflammatory signs in three months in 89.5% of patients with *L. aethiopican* [12]. However, this treatment should be reserved for patients with severe and diffuse leishmaniasis because of the severe side effects reported in patients taking this medication. These include myalgia (29-56%), cardiotoxicity presenting as T-wave inversions (9%), hepatotoxicity (44-75%), and pancreatic enzyme elevation (46-69%), [13]. There is currently an oral medication available for CL, miltefosine, which has shown promise as an effective treatment for *L. aethiopica* in several small clinical trials [14]. In 2014, the Food and Drug Administration (FDA) approved oral miltefosine for the treatment of CL of three species of the New World Type (*L. braziliensis, L. panamensis, L. guyanesis*) in children and adults 12 years of age and older in the United States. Unfortunately, miltefosine is largely unaffordable and unavailable to patients in endemic areas due to underproduction, leading to costs upwards of $10,000 for a one-month course of medication and therefore is prohibitively expensive to be first-line treatment in most regions [15]. Additional medication options for CL include oral ketoconazole, itraconazole, or fluconazole, which have been used internationally as a treatment for New World leishmaniasis with mixed results. A last-resort measure used only for uncontrolled infections is the effective, yet highly nephrotoxic parenteral liposomal amphotericin B [1]. Finally, some cases of CL can be treated with 1-4 sessions of local liquid nitrogen cryotherapy, which was found to have a >80% treatment success rate when used on small, recent-onset, uncomplicated lesions and had minimal harmful long-term effects. The short-term

effects of cryotherapy include local pain, vesicle formation, and hypo- or hyper-pigmentation at the treatment site that can persist for up to one year. Owing to the minimal long-term effects, cryotherapy can be a safe and effective option to treat lesions if detected early or if the lesion is not regressing [1,12]. Although treatment with IV pentavalent antimonials and liposomal amphotericin B have been successfully used to treat CL, the significant toxicities of these treatments were not warranted in this case. Other oral medications including itraconazole and miltefosine, as well as cryotherapy, local pentavalent antimonial, and simple excision were considered, but the lesion was closely observed over several months and has continued to regress. Therefore, the patient did not want to initiate unneeded medications or have any procedures as long as the papule continued to diminish.

It is essential that clinicians are aware of the clinical presentation of CL and report findings outside of endemic areas when possible to the CDC or other overseeing bodies. Although there is considerable epidemiologic data on CL, there is still no standard-of-care treatment available. This is mostly due to the lack of large, controlled studies of treatment options; most treatments are chosen depending upon local practice and availability of medications [10]. The reasoning behind the lack of research is likely twofold. CL does not have a particularly high mortality rate and the disease is endemic in impoverished villages and towns where people have no, or sporadic access to healthcare [7,10]. Although there is not a high mortality rate for CL, there can be a psychological impact on patients because of permanent facial scarring [7]. A desired priority is the development of standardized, non-toxic, orally-available therapy for CL as well as the development of a safe and economically viable prophylactic vaccine.

Conclusion

Patients who present with a new erythematous papule(s) on both exposed and unexposed skin after travel to areas endemic for CL should be evaluated with a high index of suspicion for leishmaniasis. Clinicians practicing in the southern United States, where cases of CL have been found, should also include CL on the differential of patients presenting with skin lesions [3]. Species-specific identification of *Leishmania* from lesions is important to rule out those that can lead to visceral and mucocutaneous disease, which would require intensive therapy.

Potential conflicts of interest

The authors declare no conflicts of interest.

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